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A new echocardiographic parameter of arterial stiffness in end-stage renal disease

Arterial stiffness (AS), characterized by endothelial dysfunction and/or calcification of the vessel wall [1], is increasingly recognized as an important predictor of cardiovascular (CV) morbidity and mortality in both the general population and in chronic kidney disease (CKD) patients [2, 3]. Previously it was shown that AS was increased in patients with end-stage renal disease (ESRD) [4]. Also, atherosclerosis leads to an increased arterial resistance through thickening and stiffening of the arterial wall [5]. Atherosclerotic changes in the carotid artery mirror general atherosclerosis. The carotid intima–media thickness (CIMT) was used in many studies showing accelerated atherosclerosis in patients with ESRD. Several authors found increased CIMT [6, 7] and a high prevalence of carotid plaques in dialysis patients [8, 9], and known risk factors for atherosclerosis were correlated with carotid artery lesions in chronic renal failure patients in these studies [6, 10, 11].

Pulse wave velocity (PWV) measured between the carotid and femoral artery is the gold standard for the assessment of arterial stiffness [12]. PWV was shown to be an independent risk factor for death in patients with ESRD [13] However, the defined procedures for the measurement of AS, including aortic strain, aortic distensibility, as well as carotid femoral [12] or aortofemoral PWV [14], are time consuming and not practical in daily practice.

It has been shown that color M-mode-derived propagation velocity measured along the origin of the descending thoracic aorta (aortic propagation velocity, APV) is associated with atherosclerosis [15], coronary artery disease [14], type 2 diabetes mellitus [16], and coronary slow flow [17]. It has been thought that increased aortic resistance secondary to atherosclerosis may be reflected with a decrease in the flow propagation speed within the arterial lumen in these studies.

The aim of our study was to investigate the relationship between APV and atherosclerosis, and whether APV can be used as a parameter of AS in patients with ESRD.

Patient and methods

The study population included 50 patients with ESRD who were treated with hemodialysis (n=23) or peritoneal dialysis (n=27) and 70 age- and sex-matched control subjects. Exclusion criteria included severe coronary artery disease, aortic aneurysm, severe valvular heart disease, left ventricular ejection fraction <40%, atrial fibrillation, frequent premature beats, left bundle branch block, and inadequate echocardiographic image quality. The study was approved by the local ethics committee. All participants were informed about the study and their consent was obtained.

Transthoracic echocardiographic examination

Echocardiographic examination was performed at rest, with the patient in the left lateral decubitus position, using a commercially available echocardiographic device (Vivid 3, General Electric, Chicago, IL, USA) with a 3.0-MHz transducer according to established standards [15], by two experienced echocardiographers who were blinded to the clinical data and ongoing therapy. From a suprasternal window, in a supine position, color M-mode Doppler recordings were obtained with the cursor parallel to the main flow of direction in the descending aorta. The color Doppler Nyquist limit was adapted to 30–50 cm/s, switching to the M-mode with a recorder sweep rate of 200 mm/s; an M-mode spatiotemporal velocity map in the shape of a flame is displayed in **Fig. 1**. If the slope of the flame was unclear, baseline shifting was used to change the aliasing velocity until a clear delineation of the isovelocity slope was seen. The aortic flow propagation velocity was then calculated from dividing the distance between points corresponding to the beginning and end

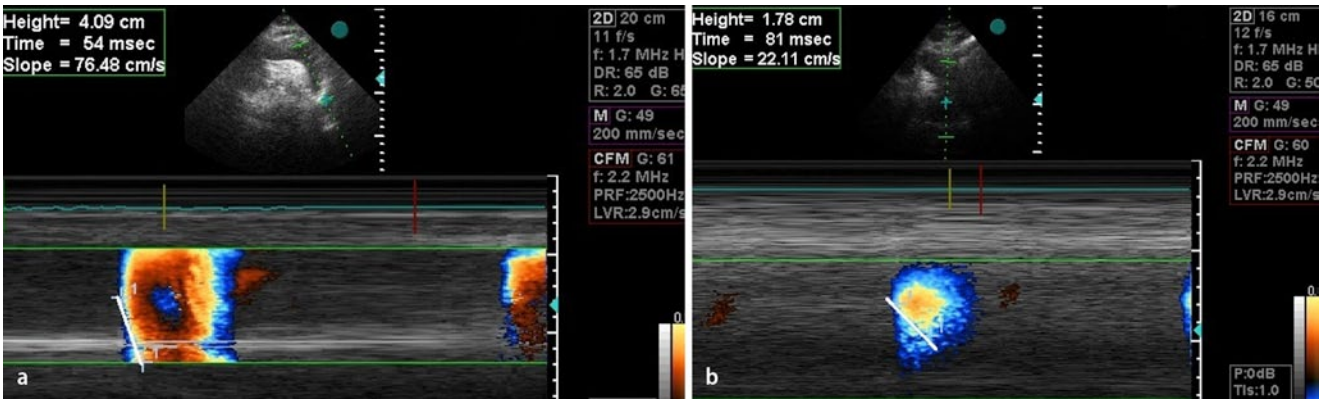

Fig. 1 ▲ Measurement of descending aorta propagation velocity (APV) in a control group patient (**a**) and in a patient with end-stage renal disease (**b**)

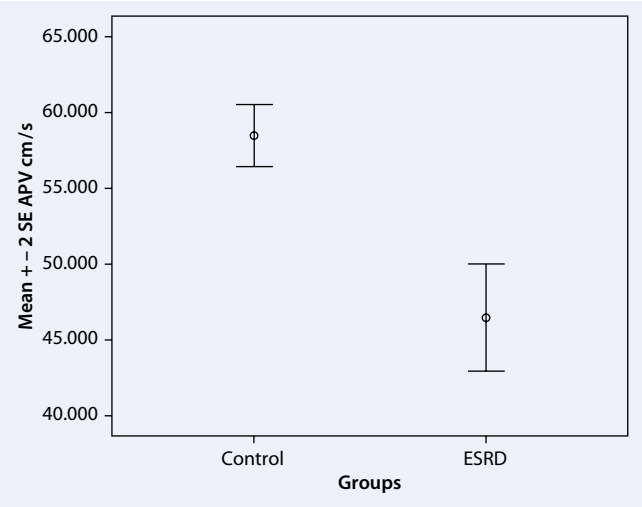

Fig. 2 ◀ Error bar of APV measurements in patients with end-stage renal disease (*ESRD*) and control group patients. *APV* color M-mode propagation velocity of descending aorta, *SE* standard error

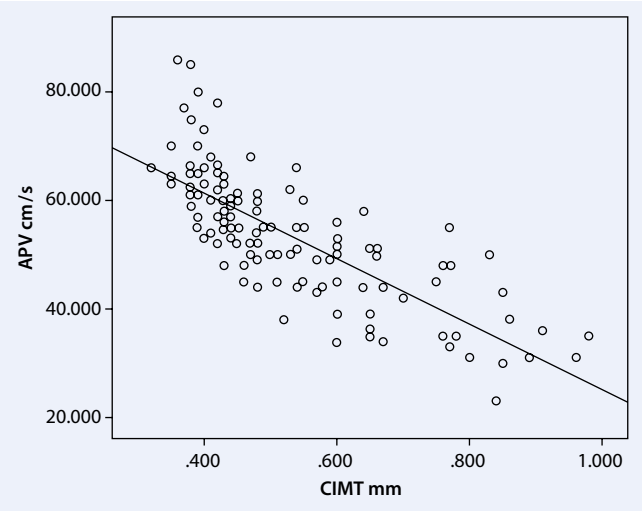

Fig. 3 ◀ Scatter plot of APV for CIMT measurements. *APV* aortic propagation velocity, *CIMT* carotid intima-media thickness

of the propagation slope by the duration between corresponding time points. Thus, APV corresponds to the velocity at which the flow is propagating down the artery. The mean of at smallest three measurements was recorded as the APV value.

CIMT measurements

The subjects' bilateral common carotid arteries were scanned longitudinally with a 7-MHz transducer attached to an available machine (Vivid 3, General Electric). The bulb dilation served as a landmark to indicate the border between the distal common carotid artery and the carotid bulb. Images were obtained from the distal portion of the common carotid artery, 1–2 cm proximal to the carotid bulb. The two bright echogenic lines in the arterial wall were identified as the intima and media lines. The intima–media thickness was measured as the distance from the main edge of the first to the main edge of the second echogenic line. Only far wall intima-media thickness of the distal 1 cm portion of the common carotid artery, just before bifurcation, was measured at end diastole (peak of the R wave of ECG). Images showing the maximum intima–media thickness were stored in a digitized fashion and CIMT measurements were made offline. Each measurement was repeated three times and the mean of the left and right common carotid arteries was used for analysis. Plaques, defined as ≥50% localized thickening of the intima compared to the rest of the wall or as an endoluminal protrusion of the arterial lumen of ≥0.5 mm, were not included in the CIMT measurement.

Pulse wave velocity

Pulsed-wave Doppler recordings were acquired from the descending thoracic artery at the origin of the subclavian artery and the left common femoral artery in supine position. Wavefront arrival at each location was defined by extrapolation of the ascending Doppler flow profile to the baseline using the electrocardiographic R wave as a time reference. The descending

aortofemoral PWV was determined by dividing the distance (measured on the body surface using a tape measure) by the time delay between two points [18]. The mean of five successive readings to cover a complete respiratory cycle was used in the analysis.

Statistical analysis

Quantitative variables are expressed as mean ± standard deviation and qualitative variables as numbers and percentages. Differences between independent groups were assessed by Student's t test for normally distributed quantitative variables, Mann–Whitney's U test for variables without a normal distribution, and the chi-square test for qualitative variables. Pearson's correlation analysis was used to assess the correlations between variables. All tests were performed with SPSS for Windows, version 10.0. All results were considered statistically significant at the level of $p<0.05$.

Results

The clinical and echocardiographic characteristics of ESRD patients and the control group are presented in **Tab. 1**. Compared to control subjects, patients with ESRD had significantly lower APV (46.4±12.4 vs. 58.5±8.5, $p<0.01$, **Fig. 2**) and higher PWV (10.5±2.5 vs. 9.2±1.2, $p<0.01$) and CIMT (0.66±0.15 vs. 0.43±0.06, $p<0.01$) measurements (**Tab. 2**). There were significant correlations between APV and CIMT ($r=-0.769$, $p<0.001$) (**Fig. 3**), APV and PWV ($r=-0.682$, $p<0.001$) (**Fig. 4**), and PWV and CIMT ($r=0.564$, $p<0.001$). There were no significant differences in APV and PWV between peritoneal dialysis and hemodialysis patients (**Tab. 3**).

Discussion

In this study, we found that APV, a new echocardiographic parameter, is decreased in patients with ESRD and significantly correlated with PWV and CIMT measurements.

Cardiovascular disease is the leading cause of death among patients with ESRD [19]. The reasons are multifacto-

Abstract · Zusammenfassung

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A new echocardiographic parameter of arterial stiffness in end-stage renal disease

Abstract

Background. Cardiovascular disease is the leading cause of death among patients with end-stage renal disease (ESRD). Arterial stiffness is an independent predictive parameter of overall and cardiovascular mortality in these patients. However, the defined procedures for the measurement of arterial stiffness are time consuming and not practical in daily practice.

Methods. The study population included 50 patients with ESRD who were treated with hemodialysis (HD; n=23) or peritoneal dialysis (PD; n=27) and 70 age- and sex-matched control subjects. Aortofemoral pulse wave velocity (PWV), carotid intima–media thickness (CIMT), and color M-mode propagation velocity of the descending aorta (aortic propagation velocity, APV) were measured.

Results. Compared to the control group, the patients with ESRD had significantly lower APV (46.4±12.4 vs. 58.5±8.5, $p<0.01$) and higher PWV (10.5±2.5 vs. 9.2±1.2, $p<0.01$) and CIMT (0.66±0.15 vs. 0.43±0.06, $p<0.01$) measurements. There were significant correlations between APV and CIMT ($r=-0.769$, $p<0.001$), APV and PWV ($r=-0.682$, $p<0.001$), and PWV and CIMT ($r=0.564$, $p<0.001$). There were no significant differences in APV and PWV between the PD and HD patients.

Conclusion. Arterial stiffness is an important indicator of atherosclerosis and arterial aging in patients with ESRD. The measurement of APV is an easy and practical new echocardiographic method and may be used to identify arterial stiffness in these patients.

Keywords

Aortic propagation velocity · Arterial stiffness · End-stage renal disease · Pulse wave velocity · Echocardiography

Neuer Echokardiographieparameter für arterielle Steifigkeit bei terminaler Niereninsuffizienz

Zusammenfassung

Hintergrund. Kardiovaskuläre Erkrankungen sind die Haupttodesursache bei Patienten mit terminaler Niereninsuffizienz (ESRD). Die arterielle Steifigkeit (AS) ist ein unabhängiger prädiktiver Parameter für die Gesamtmortalität und die kardiovaskulär bedingte Mortalität bei diesen Patienten. Allerdings sind die definierten Verfahren zur Messung der AS zeitraubend und innerhalb der täglichen Routine nicht praktikabel.

Methoden. Die Studienpopulation umfasste 50 Patienten mit ESRD, welche mittels Hämodialyse (n=23) oder Peritonealdialyse (n=27) behandelt wurden, sowie 70 nach Alter und Geschlecht entsprechend ausgewählte Kontrollen. Gemessen wurden die aortofemorale Pulswellengeschwindigkeit (PWV), die Karotis-Intima-Media-Dicke (CIMT) und die Propagationsgeschwindigkeit der Aorta descendens („aortic propagation velocity", APV) im Farbdoppler-M-Modus.

Results. Im Vergleich der Patienten mit den Kontrollen wiesen die Patienten mit ESRD eine signifikant niedrigere APV (46,4±12,4 vs. 58,5±8,5; $p<0,01$) und höhere PWV (10,5±2,5 vs. 9,2±1,2; $p<0,01$) sowie CIMT (0,66±0,15 vs. 0,43±0,06; $p<0,01$) auf. Es bestanden signifikante Korrelationen zwischen APV und CIMT ($r=-0,769$; $p<0,001$), APV und PWV ($r=-0,682$; $p<0,001$) sowie PWV und CIMT ($r=0,564$; $p<0,001$). Signifikante Unterschiede fanden sich bei APV, PWV sowie zwischen PD- und HD-Patienten nicht.

Schlussfolgerung. Die AS stellt einen bedeutenden Indikator für Atherosklerose und arterielle Alterung bei Patienten mit ESRD dar. Die Messung der APV ist ein einfaches und praktikables neues echokardiographisches Verfahren und kann zur Bestimmung der AS bei solchen Patienten eingesetzt werden.

Schlüsselwörter

Aortale Propagationsgeschwindigkeit · Arterielle Steifigkeit · Terminale Niereninsuffizienz · Pulswellengeschwindigkeit · Echokardiographie

Tab. 1 Clinical and echocardiographic characteristics of patients with ESRD and control groups

	ESRD group	Control group	p value
Age, years	42.5±16.3	37.9±12.6	NS
Men, n (%)	23 (46.0)	32 (45.7)	NS
Hypertension, n (%)	22 (44)	15 (21.4)	<0.05
Diabetes, n (%)	10 (20)	7 (10)	NS
Smoking	12 (24)	21 (30)	NS
BMI, kg/m^2	26.5±5.0	24.6±5.4	NS
SBP, mmHg	123.2±21.4	112.0±11.4	<0.05
DBP, mmHg	77.8±14.5	70.2±8.4	<0.05
Total cholesterol (mg/dl)	185.8±58.7	175.5±37.6	NS
LDL cholesterol (mg/dl)	109.9±37.0	102.1±29.5	NS
HDL cholesterol (mg/dl)	39.4±10.7	42.7±10.0	NS
Triglyceride (mg/dl)	215.8±122.3	184.9±102.9	NS
DT (ms)	253.4±66.7	204.9±32.2	**<0.01**
IVRT (ms)	116.6±18.3	87.5±13.6	**<0.01**
LV ejection fraction (%)	63.5±4.3	64.5±3.0	NS

ESRD end-stage renal disease, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein, *DT* deceleration time, *IVRT* isovolumetric relaxation time, *LV* left ventricular, *NS* not significant

Tab. 2 Comparison of measured APV, PWV, and CIMT in patients with ESRD and control group

	ESRD group	Control group	p value
APV (cm/s)	46.4±12.4	58.5±8.5	**<0.01**
CIMT (mm)	0.65±0.14	0.43±0.06	**<0.01**
PWV (m/s)	10.5±2.5	9.2±1.2	**<0.01**

APV aortic propagation velocity, *PWV* pulse wave velocity, *CIMT* carotid intima–media thickness, *ESRD* end-stage renal disease

Tab. 3 Comparison of measured APV, PWV, and CIMT in patients treated with hemodialysis and Peritoneal dialysis

	HD	PD	p value
APV (cm/s)	47.0±9.6	46.0±14.6	NS
CIMT (mm)	0.71±0.14	0.61±0.13	NS
PWV (m/s)	10.3±2.9	10.7±2.0	NS

APV aortic propagation velocity, *PWV* pulse wave velocity, *CIMT* carotid intima–media thickness, *HD* hemodialysis, *PD* peritoneal dialysis

rial, and include alterations of calcium-phosphate homeostasis and lipid metabolism, chronic inflammation, volume retention, systemic hypertension, increased oxidative stress, and chronic anemia, leading together to accelerated arteriosclerosis and atherosclerosis [13, 20]. Therefore, the arterial system in these patients undergoes structural remodeling, which is in many aspects similar to aging and is characterized by dilation, hypertrophy, and stiffening of the aorta and major arteries [7].

It has previously been shown that arterial stiffness is an independent predictive parameter for overall and cardiovascular mortality in patients with ESRD [13]. Valuable information on arterial stiffness can be obtained from noninvasive measurement of the PWV [13, 21]. PWV may represent an integrated index of vascular status and cardiovascular risk [22, 23]. An increase in PWV was established as a useful measure to characterize arterial stiffness in ESRD [24, 25]. It has been shown that increased PWV is a sign of increased arterial stiffness even in children with ESRD [26].

Atherosclerosis leads to an increased arterial resistance through thickening and stiffening of the arterial wall [5]. Arterial stiffness has been shown to be associated with coronary artery disease [27, 28] and cardiovascular risk factors such as smoking [29], obesity, hypertension [30, 31], hypercholesterolemia [32], diabetes [30, 33], and advanced age [34]. Additionally, an increase in CIMT is another risk factor for general atherosclerosis and coronary artery disease [35]. A significant increase in CIMT has been shown in ESRD [7, 36, 37]. In concordance with previous studies, we found that PWV and CIMT were significantly increased in patients with ESRD compared with age- and sex-matched control subjects.

Color M-mode propagation velocity measured along the origin of the descending thoracic aorta may reflect atherosclerosis [15]. A significant association between APV and CIMT has been shown in patients who have significant coronary atherosclerosis [38] or subclinical atherosclerosis [16]. In a recent study, we evaluated aortic strain, aortic distensibility, aortofemoral PWV, and APV in 127 patients undergoing coronary angiography. We found that among clinical and echocardiographic variables, APV was the most significant predictor of coronary artery disease and was significantly correlated with the measurements of aortic stiffness, including aortic strain, aortic distensibility, and aortofemoral PWV [14]. These findings show that the APV could be used as an indicator of arterial stiffness. In this study, we found that APV was correlated with both PWV and CIMT. Although several studies have addressed the methodological issues in various ultrasonographic indices of arterial stiffness, the reported methods — including aortic distensibility, compliance, pulse pressure, augmentation index and PWV — are difficult to use in daily practice [21, 27, 39, 40, 41]. However, measurement of APV is easy and not so time consuming compared with previous methods and it does not carry additional costs for daily practice.

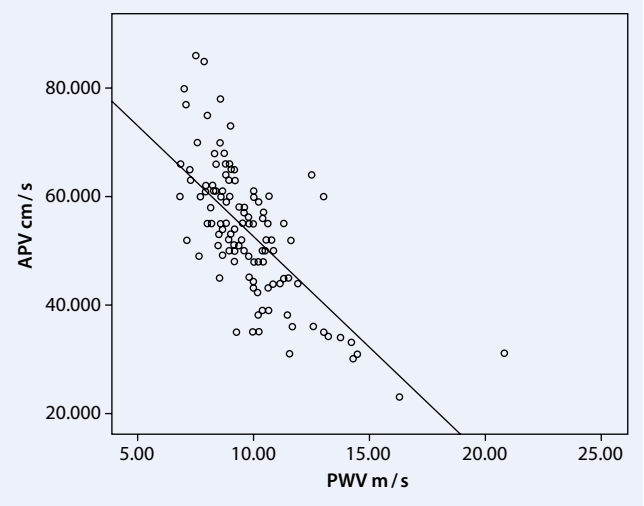

Fig. 4 ◀ Scatter plot of APV for PWV measurements. *APV* aortic propagation velocity, *PWV* pulse wave velocity

Limitations

Limited echocardiographic image quality may be an obstacle to the measurement of APV and the reproducibility of the acquisition, and reading of the methods may constitute a limitation. Aortic anatomy and loading conditions may have an impact on measurements. The small size of our study population might have biased the statistical results. To confirm the applicability of the method as a screening method, large population studies are needed. Additionally, because of ethical considerations, patients were studied under concurrent medications, and this might have had an influence on the precision of the measurements. However, low APV measurements may at least give an idea of the arterial stiffness, which is an indicator of atherosclerosis and/or arterial aging.

Conclusion

Transthoracic echocardiographic determination of the color M-mode propagation velocity of the descending aorta is a simple, practical method and correlates well with the presence of PWV and CIMT. This new parameter may be particularly useful in identifying arterial stiffness in patients with ESRD.

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Conflict of interest. On behalf of all authors, the corresponding author states that there are no conflicts of interest.

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